General

Guideline Title

Management of schizophrenia. A national clinical guideline.

Bibliographic Source(s)

Scottish Intercollegiate Guidelines Network (SIGN). Management of schizophrenia. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2013 Mar. 64 p. (SIGN publication; no. 131). [200 references]

Guideline Status

This is the current release of the guideline.

Any amendments to the guideline in the interim period will be noted on Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 10, 2016 – Olanzapine : The U.S. Food and Drug Administration (FDA) is warning that the antipsychotic medicine olanzapine can cause a rare but serious skin reaction that can progress to affect other parts of the body. FDA is adding a new warning to the drug labels for all olanzapine-containing products that describes this severe condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
- May 3, 2016 – Aripiprazole (Abilify, Abilify Maintena, Aristada) : The U.S. Food and Drug Administration (FDA) is warning that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex have been reported with the use of the antipsychotic drug aripiprazole (Abilify, Abilify Maintena, Aristada, and generics). These uncontrollable urges were reported to have stopped when the medicine was discontinued or the dose was reduced. These impulse-control problems are rare, but they may result in harm to the patient and others if not recognized.

Recommendations

Major Recommendations

Note from the Scottish Intercollegiate Guidelines Network (SIGN) and National Guideline Clearinghouse (NGC): In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the full-text guideline document.

The grades of recommendations (A–D) and levels of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are defined at the end of the "Major Recommendations" field.

Access and Engagement

Early Intervention Services

A - Individuals in the first episode of psychosis should receive treatment within the context of a specialist early intervention model of care. This should be multidisciplinary and encompass:

- Engagement/assertive outreach approaches
- Family involvement and family interventions
- Access to psychological interventions and psychologically informed care
- Vocational/educational interventions
- Access to antipsychotic medication

Assertive Community Treatment

B - Assertive outreach should be provided for people with serious mental disorders (including for people with schizophrenia) who make high use of inpatient services, who show residual psychotic symptoms and who have a history of poor engagement with services leading to frequent relapse and/or social breakdown (for example homelessness).

Specialist Ethnic Mental Health Services

D - Healthcare professionals inexperienced in working with people with schizophrenia from diverse ethnic and cultural backgrounds should seek advice and supervision from healthcare professionals who are experienced in working transculturally.

D - When working with people with schizophrenia and their carers:

- Avoid using clinical language, or keep it to a minimum
- Ensure that comprehensive written information is available in the appropriate language and in audio format if possible
- Provide and work proficiently with interpreters if needed
- Offer a list of local education providers who can provide English language teaching for people who have difficulties speaking and understanding English

Pharmacological and Related Approaches

Management of Adverse Effects

Movement Disorders

Extra-pyramidal Side Effects (EPSE)

B - If EPSE are of particular concern to a service user then second-generation antipsychotics (SGAs) or low potency first-generation antipsychotics (FGAs) should be considered.

Tardive Dyskinesia (TD)

B - Where TD is a specific concern, an SGA should be considered.

Sedation

B - If sedation is a concern, then haloperidol or aripiprazole should be considered.

Weight Gain

A - Haloperidol, aripiprazole or amisulpride should be considered for service users who are particularly concerned about weight gain, or who may be at the greatest risk of weight gain.

Behavioural Lifestyle Approaches

A - Lifestyle interventions (incorporating physical activity, dietary change and behavioural components) should be considered for service users who are experiencing weight gain on antipsychotic medications.

Metformin

B - Metformin should be considered for service users who are experiencing weight gain on antipsychotic medications.

Initial Treatment in First Episode Psychosis

Efficacy

A - Individual prescribing for service users in the first episode of psychosis should consider benefits and harms.

Treatment Strategy

D - Following initiation of an antipsychotic medication for service users in the first episode of psychosis, the medication should be continued for at least two weeks unless there are significant tolerability issues. Assessment of dose and response should be monitored during the early phase of prescribing.

D - Where there is poor response to medication there should be an assessment of medication adherence and inter-current substance misuse before the lack of response can be definitively established.

D - If there is no response to medication after four weeks, despite dose optimisation, a change in antipsychotic should be considered.

D - Where there is partial response, this should be re-assessed after eight weeks unless there are significant adverse effects.

Dose

D - Minimum effective dose of either first- or second-generation antipsychotics should be used in individuals in the first episode of schizophrenia.

Duration of Treatment

D - Following remission of the first episode of schizophrenia, the duration of maintenance treatment with antipsychotics should be at least 18 months.

Treating Acute Exacerbation or Recurrence

Efficacy

A - In service users with an acute exacerbation or recurrence of schizophrenia prescribers should consider amisulpride, olanzapine or risperidone as the preferred medications with chlorpromazine and other low-potency first-generation antipsychotics providing suitable alternatives. Consideration should be given to previous response to individual antipsychotic medications and relative adverse effect profiles.

Treatment Strategies

D - Following initiation of an antipsychotic medication for acute exacerbation of schizophrenia, the medication should be continued for at least four weeks unless there are significant tolerability issues.

D - Where a partial response is seen after review at four weeks, the medication should be re-assessed after eight weeks unless there are significant adverse effects.

Treatment to Prevent Relapse During Remission

Efficacy of Antipsychotics in Service Users Who Are in Remission

A - Individuals with schizophrenia which is in remission should be offered maintenance treatment with an antipsychotic medication.

B - For maintenance treatment, prescribers should consider amisulpride, olanzapine or risperidone as the preferred medications with chlorpromazine and other low-potency first-generation antipsychotics providing suitable alternatives.

Dose

B - Individuals with schizophrenia, which is in remission, should be offered maintenance treatment with antipsychotic medication at low to moderate regular dosing of around 300-400 mg of chlorpromazine, 4-6 mg of risperidone, or their equivalents daily.

Duration of Treatment

A - Individuals with schizophrenia which is in remission should be offered maintenance treatment with antipsychotic medication for a minimum of two years.

Delivery of Antipsychotic Medication

B - Individuals with schizophrenia who request depot and those with medication adherence difficulties should be offered maintenance treatment with depot antipsychotic medication.

Treatment-Resistant Schizophrenia

Effectiveness of Antipsychotic Medications

A - Clozapine should be offered to service users who have treatment-resistant schizophrenia.

B - Clozapine should be considered for service users whose schizophrenia has not responded to two antipsychotics including a second-generation antipsychotic medication.

Clozapine Augmentation with Another Antipsychotic

C - A trial of clozapine augmentation with a second SGA should be considered for service users whose symptoms have not responded adequately to clozapine alone, despite dose optimisation. Treatment should be continued for a minimum of ten weeks.

Clozapine Augmentation with Other Medications

B - A trial of clozapine augmentation with lamotrigine may be considered for those service users whose symptoms have had an insufficient response to clozapine alone.

High Dose Antipsychotic Medication

D - Prescribing high dose antipsychotics should only be considered after adequate trials of antipsychotic monotherapy and augmentation, including a trial of clozapine, has failed.

Electroconvulsive Therapy (ECT)

C - ECT should only be considered in those individuals for whom other approaches to treatment have failed. It may be a useful adjunct to antipsychotic medication if there is a need for rapid improvement and reduction of symptoms, or when an individual has shown a limited response to antipsychotic medication.

Specific Clinical Issues

Aggression and Hostility

D - The choice of medication for the treatment of irritability, hostility and aggression should be based on service user preference, past experience of antipsychotic treatment, the adverse effect profile and concurrent medical history. For individuals with treatment-resistant schizophrenia accompanied by aggression/hostility, a trial of clozapine is indicated.

Cognitive Dysfunction

B - Acetylcholinesterase inhibitors may be considered as adjunctive therapies to antipsychotic medication in service users where there is significant concern regarding cognitive dysfunction.

Negative Symptoms

B - For service users with persistent negative symptoms despite adherence to antipsychotic medication, consider augmentation with an antidepressant, lamotrigine, or sulpiride.

Medication Effects on Comorbidities

Comorbid Depressive Symptoms

B - Second-generation antipsychotics should be considered for individuals with schizophrenia which is in remission who have comorbid depressive symptoms.

Psychological Therapies

Adherence Therapy

B - Adherence therapy should not be offered to individuals diagnosed with schizophrenia.

Arts Therapies

B - Group based art therapy should not be routinely offered to individuals diagnosed with schizophrenia.

Cognitive Behavioural Therapy for Psychosis (CBTp)

A - Individual CBTp should be offered to all individuals diagnosed with schizophrenia whose symptoms have not adequately responded to antipsychotic medication and where persisting symptoms and/or depression are being experienced. CBTp can be started during the initial phase, the acute phase or recovery phase including inpatient settings.

B - The minimum dose of CBTp should be regarded as 16 planned sessions.

Cognitive Remediation

B - Cognitive remediation therapy may be considered for individuals diagnosed with schizophrenia who have persisting problems associated with cognitive difficulties.

Family Intervention

A - Family intervention should be offered to all individuals diagnosed with schizophrenia who are in close contact with or live with family members and should be considered a priority where there are persistent symptoms or a high risk of relapse. Ten sessions over a three month period should be considered the minimum effective dose. Family intervention should encompass:

- Communication skills
- Problem solving
- Psychoeducation

Psychoeducation

B - Psychoeducation should not be offered as a stand-alone treatment intervention to individuals diagnosed with schizophrenia.

Social Skills Training

B - Social skills training may be considered for individuals diagnosed with schizophrenia who have persisting problems related to social skills.

Perinatal Issues

Interventions to Reduce Risk of Relapse of Illness

D- Women at high risk of postnatal major mental illness should have a detailed plan for their late pregnancy and early postnatal psychiatric management, agreed with the woman and shared with maternity services, the community midwifery team, general practitioner (GP), health visitor, mental health services and the woman herself. With the woman's agreement, a copy of the plan should be kept in her hand held records. The plan should identify what support should be in place and who to contact if problems arise, together with their contact details (including out-of-hours), and address decisions on medication management in late pregnancy, the immediate postnatal period and with regard to breastfeeding.

Effects of Antipsychotic Medication on Fetal and Infant Outcomes

D - All women with childbearing potential who take psychotropic medication should be made aware of the potential effects of the medications in pregnancy. The use of reliable contraceptive methods should be discussed.

Effects on Fetal Growth and Pregnancy Metabolism

C - Women taking antipsychotics during pregnancy should be treated as high risk for gestational diabetes and monitored for blood glucose

abnormalities.

Breastfeeding

D - Women who are taking clozapine should not breast feed.

Definitions:

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+: Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies (e.g., case reports, case series)

4: Expert opinion

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review, or randomised controlled trial (RCT) rated as 1++ and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Schizophrenia

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Psychiatry

Psychology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Occupational Therapists

Pharmacists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Guideline Objective(s)

To provide evidence-based recommendations for the care and treatment of adults with schizophrenia

Note: The original guideline document does not provide specific recommendations for the following:

- Patients with at-risk or ultra-high risk mental states
- Patients with specific comorbidities such as learning disabilities or autism spectrum disorders
- Prodromal syndromes
- Transitions from child and adolescent mental health services
- Transitions to older adults services
- Particular care settings (e.g. forensic, inpatient or outpatient units, primary or secondary care)

Target Population

Interventions and Practices Considered

Access and Engagement

1. Early intervention services
2. Assertive community treatment
3. Specialist ethnic mental health services

Pharmacological and Related Approaches

1. Consideration of antipsychotic tolerability
2. Physical health monitoring
3. Management of adverse effects (movement disorders, weight gain, sedation)
4. Initial treatment in first episode psychosis (first- or second-generation antipsychotic agents)
5. Assessment of dose, response and adverse effects
6. Treatment duration

Treating Acute Exacerbation or Recurrence

1. Amisulpride, olanzapine or risperidone (preferred), chlorpromazine, other low-potency first-generation antipsychotics
2. Review and reassessment

Treatment to Prevent Relapse During Remission

1. Maintenance treatment (amisulpride, olanzapine or risperidone [preferred], chlorpromazine, other low-potency first-generation antipsychotics)
2. Duration of maintenance treatment (minimum of 2 years)

Treatment-Resistant Schizophrenia

1. Clozapine
2. Clozapine augmentation with another antipsychotic
3. Clozapine plus lamotrigine
4. High dose antipsychotics
5. Electroconvulsive therapy

Specific Clinical Issues

1. Aggression and hostility (clozapine)
2. Cognitive dysfunction (acetylcholinesterase inhibitors)
3. Negative symptoms (antidepressant, lamotrigine, or sulpiride)
4. Comorbid depressive symptoms (second-generation antipsychotics)

Psychological Therapies

1. Adherence therapy (not recommended)
2. Group-based art therapy (not routinely recommended)
3. Cognitive behavioural therapy for psychosis
4. Cognitive remediation
5. Family intervention
6. Psychoeducation
7. Social skills training

Note: The following therapies were considered, but no recommendations for their use were made: contingency management, counselling and supportive therapy, psychodynamic psychotherapy.

Perinatal Issues

1. Interventions to reduce risk of relapse of illness (establishment of a detailed plan for late pregnancy and early postnatal psychiatric management)
2. Discussion of the potential effects of psychotropic medication in pregnancy and use of reliable contraceptive methods
3. Monitoring of women taking antipsychotics during pregnancy for gestational diabetes and blood glucose abnormalities
4. Avoidance of breastfeeding in women taking clozapine

Major Outcomes Considered

- Symptom control (positive or negative psychotic symptoms and general symptoms including mood)
- Adherence to treatment regimen
- Incidence of relapse
- Frequency and length of hospitalizations
- Quality of life
- Global functioning
- Engagement in educational and/or vocational tasks

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Literature Review

The evidence base for this guideline was synthesised in accordance with Scottish Intercollegiate Guidelines Network (SIGN) methodology. The evidence base underpinning National Institute for Health and Clinical Excellence (NICE) guideline CG82 Schizophrenia: core interventions in the treatment and management of schizophrenia in adults in primary and secondary care (March 2009) was updated to form the evidence base for development of this guideline. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Evidence and Information Scientist. Databases searched include Medline, Embase, Cinahl, PsycINFO and the Cochrane Library. The year range covered was 2008-2011. Internet searches were carried out on various websites including the US National Guidelines Clearinghouse. The main searches were supplemented by material identified by individual members of the development group.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

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1-: Meta-analyses, systematic reviews, or RCTs with a high risk of bias

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2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies (e.g., case reports, case series)

4: Expert opinion

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. The result of this assessment will affect the level of evidence allocated to the paper, which will in turn influence the grade of recommendation that it supports.

The methodological assessment is based on a number of key questions that focus on those aspects of the study design that research has shown to have a significant influence on the validity of the results reported and conclusions drawn. These key questions differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. Scottish Intercollegiate Guidelines Network (SIGN) has based its assessments on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health, which have been subjected to wide consultation and evaluation. These checklists were subjected to detailed evaluation and adaptation to meet SIGN's requirements for a balance between methodological rigour and practicality of use.

The assessment process inevitably involves a degree of subjective judgment. The extent to which a study meets a particular criterion - e.g., an acceptable level of loss to follow up - and, more importantly, the likely impact of this on the reported results from the study will depend on the clinical context. To minimise any potential bias resulting from this, each study must be evaluated independently by at least two group members. Any differences in assessment should then be discussed by the full group. Where differences cannot be resolved, an independent reviewer or an experienced member of SIGN Executive staff will arbitrate to reach an agreed quality assessment.

Evidence tables are compiled by SIGN executive staff based on the quality assessments of individual studies provided by guideline development group members. The tables summarise all the validated studies identified from the systematic literature review relating to each key question. They are presented in a standard format to make it easier to compare results across studies, and will present separately the evidence for each outcome measure used in the published studies. These evidence tables form an essential part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]), available from the SIGN Web site .

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Synthesising the Evidence

Guideline recommendations are graded to differentiate between those based on strong evidence and those based on weak evidence. This judgement is made on the basis of an (objective) assessment of the design and quality of each study and a (perhaps more subjective) judgment on the consistency, clinical relevance and external validity of the whole body of evidence. The aim is to produce a recommendation that is evidence-based, but which is relevant to the way in which health care is delivered in Scotland and is therefore implementable.

It is important to emphasise that the grading does not relate to the importance of the recommendation, but to the strength of the supporting evidence and, in particular, to the predictive power of the study designs from which that data was obtained. Thus, the grading assigned to a recommendation indicates to users the likelihood that, if that recommendation is implemented, the predicted outcome will be achieved.

Considered Judgement

It is rare for the evidence to show clearly and unambiguously what course of action should be recommended for any given question. Consequently, it is not always clear to those who were not involved in the decision making process how guideline developers were able to arrive at their recommendations, given the evidence they had to base them on. In order to address this problem, SIGN has introduced the concept of considered judgement.

Under the heading of considered judgement, guideline development groups summarise their view of the total body of evidence covered by each evidence table.

Each guideline group considers the following factors:

- Quantity, quality, and consistency of evidence
- External validity (generalisability) of studies
- Directness of application to the target population for the guideline
- Any evidence of potential harms associated with implementation of a recommendation
- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources needed to treat them in accordance with the recommendation)
- Whether, and to what extent, any equality groups may be particularly advantaged or disadvantaged by the recommendations made
- Implementability (i.e., how practical it would be for the National Health Service (NHS) Scotland to implement the recommendation)

Then the group is asked to summarise its view on all of these issues, both the quality of the evidence and its potential impact, before making a graded recommendation. This summary should be succinct, and taken together with its views of the level of evidence represent the first draft of the text that will appear in the guideline immediately before a graded recommendation.

Additional detail about SIGN's process for formulating guideline recommendations is provided in Section 6 of the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the SIGN Web site .

Rating Scheme for the Strength of the Recommendations

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review, or randomised controlled trial (RCT) rated as 1++ and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The national open meeting is the main consultative phase of Scottish Intercollegiate Guidelines Network (SIGN) guideline development.

Peer Review

All SIGN guidelines are reviewed in draft form by independent expert referees, who are asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. A number of general practitioners (GPs) and other primary care practitioners also provide comments on the guideline from the primary care perspective, concentrating particularly on the clarity of the recommendations and their assessment of the usefulness of the guideline as a working tool for the primary care team. The draft is also sent to at least two lay reviewers in order to obtain comments from the patient's perspective.

It should be noted that all reviewers are invited to comment as individuals, not as representatives of any particular organisation or group. Corporate interests, whether commercial, professional, or societal have an opportunity to make representations at the national meeting stage where they can send representatives to the meeting or provide comment on the draft produced for that meeting. Peer reviewers are asked to complete a declaration of interests form.

The comments received from peer reviewers and others are carefully tabulated and discussed with the Chair and with the guideline development group. Each point must be addressed and any changes to the guideline as a result noted or, if no change is made, the reasons for this recorded.

As a final quality control check prior to publication, the guideline and the summary of peer reviewers' comments are reviewed by the SIGN Editorial Group for that guideline to ensure that each point has been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. Each member of the guideline development group is then asked formally to approve the final guideline for publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate management of adults with schizophrenia
- Reduced relapse rates and reduced hospital readmissions

Potential Harms

- Adverse effects associated with antipsychotic medications
- Second-generation antipsychotics (SGAs) tended to be associated with fewer neurological adverse effects and first-generation antipsychotics (FGAs) with greater metabolic adverse effects, in particular weight gain

Qualifying Statements

Qualifying Statements

- This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.
- Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (MA) also known as product licence. This is known as 'off label' use.
  Medicines may be prescribed off label in the following circumstances:

  - For an indication not specified within the marketing authorization
  - For administration via a different route
  - For administration of a different dose
  - For a different patient population

  An unlicensed medicine is a medicine which does not have MA for medicinal use in humans.

  Generally the off label use of medicines becomes necessary if the clinical need cannot be met by licensed medicines within the marketing authorisation. Such use should be supported by appropriate evidence and experience.

  "Prescribing medicines outside the conditions of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability."

  The General Medical Council (GMC) recommends that when prescribing a medicine off-label, doctors should:

  - Be satisfied that such use would better serve the patient's needs than an authorised alternative (if one exists)
  - Be satisfied that there is sufficient evidence/experience of using the medicines to show its safety and efficacy, seeking the necessary information from appropriate sources.
  - Record in the patient's clinical notes the medicine prescribed and, when not following common practice, the reasons for the choice.
  - Take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring the effects of the medicine.

  Non-medical prescribers should ensure that they are familiar with the legislative framework and their own professional prescribing standards.

  Prior to any prescribing, the licensing status of a medication should be checked in the current version of the British National Formulary (BNF). The prescriber must be competent, operate within the professional code of ethics of their statutory body and the prescribing practices of their employer.

Implementation of the Guideline

Description of Implementation Strategy

Implementation of national clinical guidelines is the responsibility of each National Health Service (NHS) Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Implementation of this guideline will be encouraged and supported by the Scottish Intercollegiate Guidelines Network (SIGN). The implementation strategy for this guideline encompasses the following tools and activities:

- Identification of the key recommendations that should be prioritised for implementation
- Description of recommendations likely to have significant resource implications
- Audit tools
- Guideline and supporting materials available to download from the SIGN website
- Dissemination of a quick reference guide to all appropriate healthcare professionals
- Electronic dissemination of the full guideline to all NHS Boards
- iPhone, iPad and Android apps
- Patient version of the guideline

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Scottish Intercollegiate Guidelines Network (SIGN). Management of schizophrenia. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2013 Mar. 64 p. (SIGN publication; no. 131). [200 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Mar

Guideline Developer(s)

Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]

Source(s) of Funding

Scottish Executive Health Department

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

Guideline Development Group: Professor Andrew Gumley, Professor of Psychological Therapy, University of Glasgow (*Co-Chair*); Dr Mark Taylor, Consultant Psychiatrist, National Health Service (NHS) Lothian (*Co-Chair*); Dr Alison Blair, Consultant Psychiatrist, ESTEEM, Glasgow; Dr Roch Cantwell, Consultant Perinatal Psychiatrist, NHS Greater Glasgow and Clyde; Ms Patricia Cawthorne, Consultant Nurse in Psychological Therapies, The State Hospital, Carstairs; Dr Suzy Clark, Consultant Clinical Psychologist, ESTEEM, Glasgow; Dr Alexis Craig, General Practitioner, Elmbank Group, Aberdeen; Mrs Karen Fraser, Principal Pharmacist - Mental Health, NHS Ayrshire and Arran; Dr Helen Griffiths, Consultant Clinical Psychologist, NHS Lothian; Dr Sameer Jauhar, Specialist Registrar, General Adult Psychiatry; Ms Joanna Kelly, Evidence and Information Scientist, Scottish Intercollegiate Guidelines Network (SIGN); Professor Stephen Lawrie, Professor of Psychiatry, Edinburgh University; Mr Gordon Mitchell, Consultant Clinical Psychologist, Stratheden Hospital, Cupar; Dr Peter Rice, Consultant Psychiatrist, NHS Tayside Substance Misuse Services, Sunnyside Royal Hospital, Montrose; Professor Matthias Schwannauer, Head of Clinical Psychology, University of Edinburgh; Ms Frances Simpson, Chief Executive, Support in Mind Scotland, Edinburgh (from Jan 2012); Mrs Maureen Summers, Lay Representative, Perth; Ms Anne Suttle, Occupational Therapist, NHS Borders; Dr Lorna Thompson, Programme Manager, SIGN; Ms Mary Weir, Chief Executive, Support in Mind Scotland, Edinburgh

Financial Disclosures/Conflicts of Interest

Declarations of interests were made by all members of the guideline development group. Further details are available from the Scottish Intercollegiate Guidelines Network (SIGN) Executive.

Guideline Status

This is the current release of the guideline.

Any amendments to the guideline in the interim period will be noted on Scottish Intercollegiate Guidelines Network (SIGN) Web site.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site.

Availability of Companion Documents

The following are available:

- Quick reference guide: Management of Schizophrenia. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2013 Mar. 2 p. Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site .
- SIGN 50: A guideline developer's handbook. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network. (SIGN publication; no. 50). Available from the SIGN Web site .

Patient Resources

None available

NGC Status

This summary was completed by ECRI Institute on May 6, 2013. The information was verified by the guideline developer on June 12, 2013. This summary was updated by ECRI Institute on October, 5 2015 following the U.S. Food and Drug Administration advisory on Clozapine. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs. This summary was updated by ECRI Institute on May 24, 2016 following the U.S. Food and Drug Administration advisory on Olanzapine. This summary was updated by ECRI Institute on May 31, 2016 following the U.S. Food and Drug Administration advisory on Aripiprazole (Abilify, Abilify Maintena, Aristada).

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